PRELIMINARY AND SHORT REPORT

INHIBITION OF GRENZ RAY ERYTHEMA BY ONE SINGLE TOPICAL HORMONE APPLICATION*

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We recently reported that hydrocortisone, and to a lesser extent corticotrophin, when locally applied to the skin, inhibits the cutaneous inflammatory response to such stimuli as ultraviolet irradiation, and to such primary irritants as mustard oil. This inhibition was demonstrable only if the hormones had been applied several hours before the inflammatory stimulus was introduced. It consisted either in a complete suppression, or in a delayed and partially inhibited reaction. Our observations suggested that a protective local mechanism was involved, through which the normal tissue reaction to the secondary products of inflammation was prevented, thereby profoundly altering the entire course of tissue response.

This report describes experiments designed to investigate the possibility that a similar mechanism might affect the reactions to ionizing radiation.

MATERIALS AND METHODS

Twelve male volunteers, ranging in age from 32 to 69 years were tested; the normal skin of the upper back below the level of the scapular spine was used as test site.

Identical procedures were performed in all subjects.

1. Hydrocortisone 1%, fluorocortisone 0.2% and corticotrophin 5% in an ointment base containing glycerin, water and emulsifiers was applied in each case six hours prior to the irradiation and removed 1 hour before the radiation was applied. Only the results with hydrocortisone are tabulated. All subjects received control irradiations on areas pretreated with the empty ointment base and on not pretreated areas.

2. A Siemens grenz ray apparatus with a lithium (Lindemann) window was used. Fields of 2 cms diameter at a F.S.D. of 10 cms were treated using metal tubes. The half-value of the rays used was uniformly 0.022 mm aluminum, and doses of 950 r, 1140 r and 1360 r were administered to pretreated and control areas.

3. Initially the irradiated areas were observed every two hours until the early erythema had reached its peak; then observations were made every 2 to 3 days until the late erythema had subsided. The term "early erythema" refers to the erythema which developed a few hours after irradiation and reached its peak after about 48 hours, while the term late erythema refers to the dark cyanotic erythema which developed between the 27th and 47th day after irradiation.

RESULTS AND DISCUSSION

The alterations of the inflammatory response were comparable with those obtained previously (1) with ultraviolet irradiation and with the primary irritants. Complete suppression of the erythema response as well as partial inhibition or delay in appearance was observed.

The late erythema was altered to a greater extent than the early erythemas, the lower dosage fields showed more inhibition than the ones where a higher dose was given. Striking was the delay phenomenon particularly as observed with the late erythema. This occurred in about half of the pretreated areas and the appearance of the erythema was delayed from 4 to 19 days as compared to the control fields. In seven instances a complete inhibition of the

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late erythema occurred in the hydrocortisone pretreated fields in which 950 r were applied, while a sharply outlined dark cyanotic erythema appeared in the control sites.

The possibility of a filtering effect by the ointment base was ruled out by the controls pretreated with the empty ointment base, since these fields showed no inhibition, and by

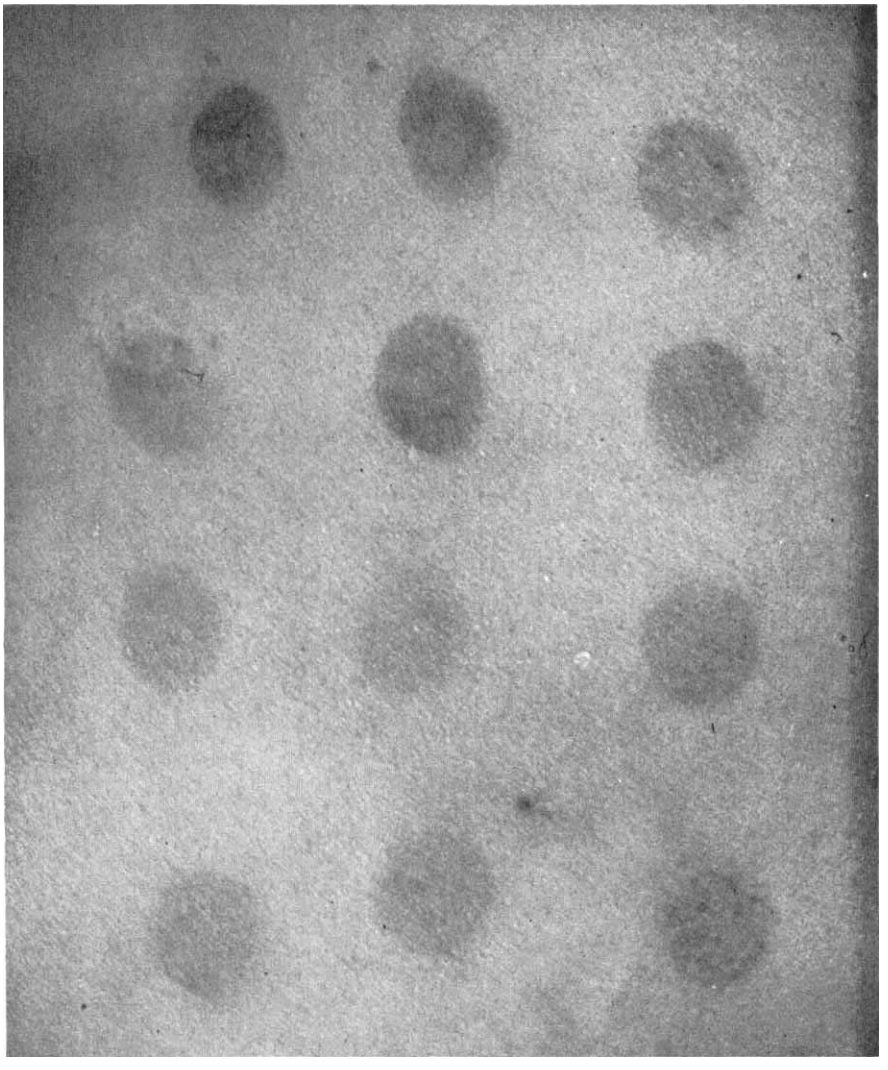

FIG. 1. This photograph was taken 41 days after irradiation. The control sites are represented in the top row. All 3 fields show an erythema. The vertical row to the right had been irradiated with 1360 r. All fields, No. 3, 6, 9, 12, show erythema, which at this date was already partially fading. The center row had been irradiated with 1140 r. Field 2 (control) and field 5, (pretreated with A.C.T.H.) show erythema. Field 8 (pretreated with hydrocortisone) and field 11 (fluorocortisone) show pigmentation only. The late erythema did not occur at any time in these fields. The erythema in field 5 (A.C.T.H.) appeared several days later than in the control field. In the vertical row to the left (950 r) erythema was absent in fields 7 and 10 and markedly inhibited in field 4.

TABLE I

The effect of the prior application of hydrocortisone on the development of grenz ray erythemata

Erythema	No. of Cases	Alteration of Maximal Degree of Erythema								
		Complete inhibition			Partial inhibition			No inhibition		
		950 r	1140 r	1360 r	950 r	1140 r	1360 r	950 r	1140 r	1360 r
Early (3–48 hr.)	12	5	1	0	1	4	0	7	7	12
Late (27–48 day)	12	7	2	0	4	6	2	1	4	10

Alteration of the Development of Erythema

Erythema	No. of cases	Delay in appearance of erythema		
		950 r	1140 r	1360 r
Early (3–48 hr.)	12	3	4	1
Late (27–48 day)	12	7	6	5

the fact that both empty ointment base and hormone containing vehicles had been thoroughly washed off prior to irradiation. N. Kanof (2) reported an ultraviolet light screening effect of hydrocortisone. This effect did not appear to be relevant in our experimental setting for the following reasons:

1. Inhibition was not obtained in those tests in which the time of contact between the hormone and the skin was too short (less than 10 minutes).

Inhibition was also not obtained in those tests in which the hormone had been applied immediately prior to the irradiation. This time relationship and our studies with labeled material suggest that the protective effect occurs only when the hormone had reached the basal layer of the epidermis.

2. The delay phenomenon observed could not be explained by a screening effect.

3. As tested with the ultraviolet experiments, the inhibitory effect persisted even after epidermal stripping, a procedure which thoroughly removes all traces of hormone from the surface.

4. Closely parallel results were obtained with ultraviolet rays, grenz rays and the primary irritants.

The natural sequence of erythema cycles following grenz ray application is well known; the erythema waves follow each other regularly and at fixed time intervals and the pattern is reproducible under similar conditions in the same individual.

So far there have been no means of altering this sequence. The physiological changes responsible for these cyclic and prolonged effects upon tissue are unknown, but one might assume that, in response to the ionizing effects of the radiation, a chain of chemical and enzymatic reactions is initiated in the tissues. Since it is more than unlikely that a short contact of a hormone with the skin prior to irradiation could prevent the destructive cellular and nuclear changes produced by Roentgen rays, we assume that the alteration in erythema response is probably due to a process that protects the cells against the effect of substances released by those destructive cellular changes.

SUMMARY

One single application of an ointment containing 1% hydrocortisone, 0.2% of fluorohydrocortisone or 5% corticotrophin, applied several hours before and removed immediately prior to irradiation with varying doses of grenz rays proved capable in a certain dosage range in either completely suppressing, or partially inhibiting or in delaying the erythema cycles ensuing in the control sites.

REFERENCES

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2. Norman B. Kanof: Observations on the effect of local applications of hydrocortisone upon thermal burns and ultraviolet erythema. Read at the 16th Annual Meeting of the Society of Investigative Dermatology, Inc., Atlantic City, N. J., June, 1955.